UCRL-JC-124568 Abs Rev 1

Identification, organization and characterization of ZNF genes in a 4 MB cluster on 19p12. Harvey W. Mohrenweiser[1], Susan M. G. Hoffman[2], Dominique Poncelet[3], Joseph Martial[3] and Evan E. Eichler[1]. [1] Human Genome Center, Lawrence Livermore National Labs, Livermore, CA, [2] Miami Ohio University, Miami, OH, [3] Laboratoire de Biologie Moleculaire et de Genie Genetique, Universite de Liege, Belgium.

Zinc finger (ZNF) genes represent one of the largest and most diverse gene families in the human genome, constituting ~ 0.01% of the human genetic material. Chromosome 19 appears to be particularly enriched for ZNF genes, with one third of all ZNF loci are distributed in three clusters corresponding to cytogenetic band locations 19p12, p13.2 and q13.4. We are currently mapping and characterizing ZNF genes of the largest tandemly duplicated gene-family (4MB) in the human genome, found in cytogenetic band 19p12. Long-range inter-Alu PCR of a contig of 19p12 YAC clones has been used to identify 300 cosmids and 15 BAC's. Nineteen cosmid contigs have been constructed comprising ~ 3.5 MB of this 4 MB interval. The location of cosmid contigs was confirmed using FISH and cosmids were anchored using an STS marker screening strategy. To define the architecture of the 19p12 ZNF cluster, probes corresponding to various ZNF91 exons were used to screen Southern blots of EcoR1-digested genomic clones . This analysis identified a minimum of 30 potential KRAB (Krueppel-related associated box) ZNF genes in this region. The genes appear to be arranged in head-to-tail organization, with duplicon sizes ranging from 100 to 180 kb. Near the promoter of virtually all 19p12 ZNF genes, human endogeneous retrovirus (HERV) elements have been identified, suggesting that these elements were tandemly duplicated with the ZNF cluster. Comparative sequencing and retroposon-mapping indicate that these duplications occurred ~ 35-50 mya. Hybridization and sequence analysis has confirmed the identity, thus far, of five functional zinc finger genes. Large scale sequence analysis has been initiated to address the organization, origin, and proliferative nature of the ZNF genes within this region.

*Performed under auspices of the US DOE by LLNL; contract No. W-7405-ENG-48.

Hugo, Human Genome Meeting, Toronto, Canada, March 6-8, 1997